

Rule B12

1. A protein produced by a method comprising:
culturing a host cell into which has been
introduced a DNA expression vector comprising the following
operably linked elements:

a DNA segment comprising a nucleotide sequence as shown in SEQ ID NO: 1 from nucleotide 76 to nucleotide 417; and

2. The protein of claim 1, wherein the host cell is a mammalian cell.

a transcription promoter;
a DNA segment encoding an endoprotease; and
a transcription terminator, wherein said host cell expresses the polypeptide encoded by the DNA segment comprising a nucleotide sequence shown in SEQ ID NO: 1 from nucleotide 76 to nucleotide 417; and said DNA segment encoding said endoprotease.

4. An isolated and purified protein comprising:
a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue 110 (Ser) or 114 (Arg); and
a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139

(Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating.

5. An isolated and purified protein comprising:
a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue selected from the group consisting of 48 (Lys), 49 (Thr) and 50 (Phe); and

a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139 (Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating.

6. A method of stimulating proliferation of pancreatic islets comprising administering to a mammal in need thereof, an amount of an isolated and purified protein comprising:

a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue 110 (Ser) or 114 (Arg); and

a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139 (Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating, sufficient to produce a clinically significant increase in insulin secretory capacity in said mammal.

7. The method of claim 6, wherein the clinically significant increase in insulin secretory capacity results in a decrease in fasting plasma glucose levels.

8. The method of claim 6, wherein the isolated and purified protein is administered in combination with an insulin sensitizer.

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a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue selected from the group consisting of 48 (Lys), 49 (Thr) and 50 (Phe); and

a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139 (Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating, sufficient to produce a clinically significant increase in insulin secretory capacity in said mammal.

10. The method of claim 9, wherein the clinically significant in insulin secretory capacity results in a decrease in fasting plasma glucose levels.

11. The method of claim 9, wherein the isolated and purified protein is administered in combination with an insulin sensitizer.

12. A method for stimulating in vitro proliferation of pancreatic islet cells comprising culturing islets with an amount of an isolated and purified protein comprising:

a first polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 26 (Ala) to residue 110 (Ser) or 114 (Arg); and

a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139 (Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating, sufficient to produce an increase in the number of islet cells as compared to islet cells cultured in the absence of said protein.

14. A method for stimulating in vitro proliferation of pancreatic islet cells comprising culturing pancreatic islets in an amount of an isolated and purified protein comprising:

a second polypeptide comprising amino acid sequence as shown in SEQ ID NO: 2 from residue 115 (Ser) to residue 139 (Thr), wherein said first polypeptide and said second polypeptide are capable of disulfide associating, sufficient to produce an increase in the number of islet cells as compared to islet cells cultured in the absence of said protein.

15. The method of claim 14, wherein said cells are cultured in 0.1 ng/ml to 100 ng/ml of said protein.